UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA PHARMACEUTICALS UK LTD.,	:	02 Civ. 7936 (WHP)
Plaintiffs,	:	03 Civ. 6487 (WHP)
-against-	:	OPINION AND ORDER
MAYNE PHARMA (USA) INC.,	:	
Defendant.	:	

WILLIAM H. PAULEY III, District Judge:

AstraZeneca Pharmaceuticals LP and AstraZeneca Pharmaceuticals UK Ltd. (collectively, "AstraZeneca") allege patent infringement by Mayne Pharma (USA) Inc. ("Mayne"), formerly known as Faulding Pharmaceutical Company. In particular, AstraZeneca accuses Mayne of infringing U.S. Patent Nos. 5,714,520 (the "'520 patent"), 5,731,355 (the "'355 patent") and 5,731,356 (the "'356 patent") (collectively, the "asserted patents") by filing Abbreviated New Drug Application ("ANDA") No. 76-452 with the United States Food and Drug Administration ("FDA").

This action arises under 35 U.S.C. § 271(e) and this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a). Venue is proper under 28 U.S.C. §§ 1391(b)-(c) and 1400(b). This Court conducted an eleven-day bench trial. Insofar as the Court exercises its prerogative as finder of fact to determine the weight and credibility of the evidence, the discussion herein is limited to the evidence that this Court credits. Further, this Court recites only those findings of fact that are relevant to its conclusions of law.

FINDINGS OF FACT

AstraZeneca owns the asserted patents. Those patents have a common specification and relate to a pharmaceutical composition of propofol and edetate. AstraZeneca alleges that by filing ANDA No. 76-452, Mayne infringed one or more claims of the asserted patents under 35 U.S.C. § 271(e)(2)(A).[1] ANDA No. 76-452 was filed by ESI Lederle ("ESI"), formerly a division of Wyeth Pharmaceuticals, Inc. ("Wyeth") and later a division of Baxter Healthcare Corporation ("Baxter"). Mayne acquired ANDA No. 76-452 from Baxter and is now the applicant of record.

I. Procedural History

By letter dated August 20, 2002, Wyeth provided notice to AstraZeneca pursuant to 21 U.S.C. § 355(j)(2)(B)(ii) that ESI was seeking FDA approval of ANDA No. 76-452, which it filed on June 28, 2002. (Plaintiffs' Exhibit ("PX") 121.) ANDA No. 76-452 indicated Wyeth's intention to commercially manufacture, use or sell its "generic propofol emulsion, 20 mL vial." (Joint Pretrial Order ("JPTO") ¶ VI.B.24.) On October 4, 2002, AstraZeneca filed the first of these consolidated actions, No. 02 Civ. 7936 (WHP), alleging patent infringement by Wyeth based on the August 20, 2002 notice. (JPTO ¶ VI.B.25.) On February 3, 2003, Mayne, was substituted as the defendant and Wyeth was dismissed from the action. (JPTO ¶ VI.B.26.)

By letter dated July 15, 2003, Mayne notified AstraZeneca pursuant to 21 U.S.C. § 355(j)(2)(B)(ii) that it was seeking FDA approval for its amended ANDA No. 76-452, filed on

[1] 35 U.S.C. § 271(e)(2)(A) provides:

> It shall be an act of infringement to submit – (A) an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act or described in section 505(b)(2) of such Act for a drug claimed in a patent or the use of which is claimed in a patent.

July 7, 2003, to engage in the commercial manufacture, use or sale of its generic propofol emulsion in 50 and 100 mL vials. (JPTO ¶ VI.B.27.) On August 6, 2003, AstraZeneca filed the second action, No. 03 Civ. 6487 (WHP), alleging patent infringement by Mayne based on its July 15, 2003 notice. (JPTO ¶ VI.B.28.) This Court consolidated the actions on October 24, 2003.

II. Background of the Claimed Inventions

By way of background, propofol is an injectable anesthetic that has hypnotic properties and can be used as a general anesthetic for sedation. AstraZeneca markets propofol under the trademark DIPRIVAN® for use in treating humans and under the trademark RAPINOVET® for veterinary use. (PX 1, Col. 1, lines 7-13.) Microbial contamination of propofol compositions can cause nosocomial infection among intensive care unit ("ICU") patients. As a result, the "giving set"[2] used to administer the earlier propofol compositions had to be changed every six to twelve hours. (PX 1, Col. 2, line 62 - Col. 3, line 3.)

AstraZeneca's approved New Drug Application ("NDA") No. 19-627 is directed to the manufacture and sale of a "propofol injectable emulsion for use in anesthesia and sedation" ("Original Diprivan"). (JPTO ¶ VI.B.2.) Original Diprivan was an oil-in-water emulsion containing one-percent 2,6-diisopropylphenol (i.e., propofol) for intravenous administration. (Trial Transcript ("Tr.") at 246-47, 259-60.) Original Diprivan did not contain an antimicrobial additive. (Tr. at 783.) Original Diprivan was launched in the United States in November 1989, following use in Europe for five to seven years. (Tr. at 59-60, 73, 349.)

[2] The "giving set" is the tube that connects an intravenous needle to the bag containing the pharmaceutical composition administered to the patient.

Soon after its launch in the United States, AstraZeneca received reports of post-operative infection among patients given Original Diprivan. AstraZeneca sought to improve Original Diprivan. In June 1990, AstraZeneca added instructions on proper handling procedures in its "package insert" and sent a special mailing to doctors regarding those instructions. In early 1991, AstraZeneca revised these procedures and recommended that unused portions of an Original Diprivan vial be discarded six hours after opening. (Tr. at 75-83; see also Tr. at 350-51; Joint Exhibit ("JX") 33 at AZ081112.)

At that time, AstraZeneca's scientists recognized that the oil in the emulsion allowed the growth of microbes introduced into the water phase of the emulsion through improper handling. (Tr. at 50-51, 350, 354; JX 33.) Soon thereafter, the inventors of the asserted patents concluded that retarding microbial growth would resolve the issue. (Tr. at 361-72; JX 32 at AZ041069-70.) The inventors came to believe that adding a small amount of disodium edetate (0.005% by weight) would provide broad antimicrobial protection for at least twenty-four hours without disrupting the oil-in-water emulsion. (Tr. at 369-77.) Thus, AstraZeneca modified Original Diprivan by adding disodium edetate to the formulation ("Modified Diprivan"). Notably, all Original Diprivan ingredients are present in Modified Diprivan, and the anesthetic properties of Original Diprivan are identical to Modified Diprivan. (Tr. at 56-58.)

The inventors filed a patent application covering their invention with the United States Patent and Trademark Office (the "USPTO") on March 22, 1995. AstraZeneca submitted a supplemental New Drug Application ("sNDA") for Modified Diprivan on December 22, 1995. The FDA approved the sNDA on June 11, 1996, and granted AstraZeneca three years of "marketing exclusivity" for Modified Diprivan. (Tr. at 101-02; PX 160 at AZ014136,

AZ014140-43.) At the same time, AstraZeneca applied to withdraw FDA approval for Original Diprivan; the FDA approved this request in 1998. (Tr. at 101-03.)

Net sales for Modified Diprivan from 1997 through 2004 have exceeded $2 billion. Despite competition from similar products on the market, AstraZeneca's sales have exceeded $200 million per year. (Tr. at 106-08; PX 257A; see Tr. at 631, 959-60.)

III. The Asserted Patents

AstraZeneca received three patents for Modified Diprivan. The '520 patent, titled "Propofol Composition Containing Edetate," was issued on February 3, 1998. Thereafter, the '355 and '356 patents, each titled "Pharmaceutical Compositions of Propofol and Edetate," issued on March 24, 1998. The '355 and '356 patents are divisional applications based on the '520 patent's disclosure. (PX 1-3.) The asserted patents have a common specification and concern a pharmaceutical composition of propofol and edetate. (JPTO ¶ VI.B.5.) The asserted claims are Claims 1-14, 16-32 and 34 of each asserted patent and Claims 38-39 of the '520 patent. (JPTO ¶ VI.B.6.)

A. The Specification

The asserted patents relate to formulaic variations of sterile propofol pharmaceutical compositions for anesthetic use. These compositions comprise an oil-in-water emulsion of propofol containing sufficient amount of edetate to retard the growth of microorganisms for over twenty-four hours if the composition becomes contaminated. (PX 1, Col. 4, lines 38-45.) The oil-in-water emulsion is a distinct two-phase system in equilibrium that is kinetically stable, but thermodynamically unstable. (PX 1, Col. 4, lines 46-50.)

During their experiments which led to the patented inventions, the inventors noted that "the addition of small amounts of a selected agent to 'Diprivan' will enable the formulation to be administered in 'giving sets' that require changing significantly less frequently than is presently the case." (PX 1, Col. 3, lines 20-25.) The inventors experimented with various additives to Original Diprivan and "unexpectedly found that edetate, which is not regarded as a broad spectrum antimicrobial agent was the only agent that would meet [their] requirements." (PX 1, Col. 4, lines 22-34.) The specification defines "edetate" as "ethylenediaminetetraacetic acid (EDTA) and derivatives thereof." (PX 1, Col. 4, lines 51-52.) The specification contains no indication that the inventors intended a narrow definition for edetate. Indeed, it states: "The nature of the edetate is not critical, . . . [as long as it] fulfils [sic] the function of preventing significant growth of microorganisms for at least 24 hours in the event of adventitious extrinsic contamination." (PX 1, Col. 4, lines 57-61.)

The inventors performed tests to determine their preferred composition for Modified Diprivan. (PX 1, Col. 7, line 1 - Col. 11, line 12.) They tested comparative microbiological activity of Original Diprivan with and without 0.005% disodium edetate. While the Original Diprivan formulation without disodium edetate failed the microbiological test, the formulation with disodium edetate passed. (PX 1, Col. 9, line 64 - Col. 10, line 32.) The specification also describes tests of comparative microbiological activity of an oil-in-water emulsion with the same formulation as Original Diprivan but containing no propofol. Here, too, the formulation without disodium edetate failed the microbiological test, while the formulation with disodium edetate passed. (PX 1, Col. 10, line 39 - Col. 11, line 10.)

B. The Asserted Claims

Claim 1 of the '520 patent is as follows:

> A sterile pharmaceutical composition for parenteral administration which comprises an oil-in-water emulsion in which propofol dissolved in a water-immiscible solvent, is emulsified with water and stabilized by means of a surfactant, and which further comprises an amount of edetate sufficient to prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours as measured by a test wherein a washed suspension of each said organism is added to a separate aliquot of said composition at approximately 50 colony forming units per ml, at a temperature in the range 20°-25° C., whereafter said aliquots are incubated at 20°-25° C. and are tested for viable counts of said organism after 24 hours, said amount of edetate being no more than 0.1% by weight of said composition.

(PX 1, Col. 11, lines 33-48.) Claim 38 is identical to Claim 1 but includes the additional requirement that the edetate not destabilize the emulsion. Claims 2 and 20 specify that the edetate is disodium edetate, and Claim 34 specifies the amount of disodium edetate as 0.005%. (PX 1, Col. 11, line 33 - Col. 14, line 36.) Claims 3-14 specify the various constituents of the Claim 1 formulation, and Claims 16-19, 21-32 and 39 address the molar concentrations of edetate.

The asserted claims of the '355 patent are directed to "[a] method for producing anaesthesia in a warm-blooded animal which comprises parenterally administering" a sterile pharmaceutical composition of the type set forth in the claims of the '520 patent. The asserted claims of the '356 patent are directed to "[a] method for limiting the potential for microbial growth" in a sterile pharmaceutical composition of the type described in the claims of the '520 patent.

Highly pertinent to the infringement analysis below, each asserted claim includes "edetate." In its Markman ruling, this Court defined "edetate" as follows:

> EDTA as well as compounds structurally related to EDTA regardless of how they are synthesized, and which can prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours.

AstraZeneca Pharmas., LP v. Mayne Pharma (USA), Inc., 352 F. Supp. 2d 403, 419 (S.D.N.Y. 2004).

IV. The Accused Formulation

AstraZeneca accuses Mayne of infringing the asserted patents by filing ANDA No. 76-452 which describes Mayne's generic propofol emulsion. Mayne's formulation, generic versions of Original Diprivan and later of Modified Diprivan, were developed by ESI. Dr. Martin Joyce led the ESI work, starting in September 1994. In 1995, ESI researchers learned about the risk of microbial infection from the improper handling of Original Diprivan. In June 1996, when ESI's researchers learned that AstraZeneca had reformulated Original Diprivan to include an antimicrobial additive, ESI also changed its generic propofol formulation to include an additive. (Tr. at 906, 928-30.) ESI filed an ANDA on the formulation in December 1996 with a "Paragraph III Certification."[3] (Tr. at 906, 908-09.)

In February 1998, ESI learned that AstraZeneca had received a patent on its Modified Diprivan formulation. (Tr. at 906.) Dr. Joyce and his colleagues read the '520 patent while continuing their work. (Tr. at 930-33, 945; PX 97.) ESI then started screening antimicrobial agents for its generic composition. (Tr. at 907.) Dr. Joyce's team considered the

[3] A Paragraph III Certification informs the FDA that the ANDA applicant is aware of a patent covering its formulation and that the applicant does not intend to market its product until the patent expires. See 21 U.S.C. § 355(j)(2)(A)(vii)(III).

option of "initiating new formulation efforts" to replace Modified Diprivan's EDTA with a different agent. (Tr. at 935.)

In an August 5, 1998 memorandum, Dr. Mary George, the senior formulator on the project, identified the calcium trisodium salt of diethylenetriaminepentaacetate ("DTPA"),[4] as a promising antimicrobial candidate for ESI's generic formulation. (Tr. at 912-13, 941-44; JX 4; JX 12.) Calcium trisodium DTPA was chosen for a number of reasons. First, the compound appeared in the FDA Inactive Ingredient Guide, which lists excipients in approved products. (Tr. at 913; JX 4.) Second, with this compound, ESI's generic formulation matched the characteristics and stability profile of Modified Diprivan, and thus was capable of being approved as an ANDA without additional clinical or safety studies. (Tr. at 944; JX 4.) Third, Dr. George believed that the addition of calcium trisodium DTPA to ESI's generic formulation did not infringe the '520 patent. (Tr. at 944-47; JX 4.) Finally, the compound satisfied the microbiological test set forth in the '520 patent. (Tr. at 947-48; JX 4.)

Mayne's generic propofol emulsion is an "intravenous sedative-hypnotic agent for use in the induction and maintenance of anesthesia or sedation in a human patient." (JPTO ¶ VI.B.20.) Mayne's formulation, a sterile pharmaceutical composition for parenteral administration, "is an oil-in-water emulsion in which propofol dissolved in a water-immiscible solvent, is emulsified with water and stabilized by means of egg lecithin as a surfactant." (JPTO ¶¶ VI.B.8-10.) Mayne's formulation "contains 1% by weight of propofol." (JPTO ¶ VI.B.11.) In addition, it contains 10% by weight of soybean oil as a water immiscible solvent. (JPTO ¶¶

[4] DTPA is also known as pentetic acid or pentetate. Calcium trisodium DTPA is also known as pentetate calcium trisodium, calcium trisodium pentetate and more commonly as Ca-DTPA. See FDA, Pentetate calcium trisodium injection, at www.fda.gov/cder/foi/label/2004/021749Ca-DTPAlbl.pdf. (See also PX 21 at FPC221291-92; PX 281 at FPC255811.) For ease of reference, this Court refers to Ca-DTPA as calcium trisodium DTPA.

VI.B.12-13.) The emulsion also contains water, sodium hydroxide and "12 mg/ml (or 1.2% by weight) of egg lecithin, a naturally occurring phosphatide, as a surfactant." (JPTO ¶¶ VI.B.14-15, 17.) The generic propofol emulsion is "made isotonic with blood by incorporation of 22.5 mg/ml (or 2.25% by weight) of glycerol." (JPTO ¶¶ VI.B.18-19.) Its pH is between 7.0 and 8.5. (JPTO ¶ VI.B.16.)

More important to the infringement analysis below, Mayne's generic propofol emulsion "contains 0.008 mg/ml (or 0.0008% by weight) of calcium trisodium DTPA as an antimicrobial agent." (JPTO ¶¶ VI.B.21, 23.) The amount of calcium trisodium DTPA is

> sufficient to prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours as measured by a test wherein a washed suspension of each said organism is added to a separate aliquot of said composition at approximately 50 colony forming units per ml, at a temperature in the range 20°-25° C., whereafter said aliquots are incubated at 20°-25° C. and are tested for viable counts of said organism after 24 hours.

(JPTO ¶ VI.B.22.)

ESI filed ANDA No. 76-452 for its proposed generic formulation on June 28, 2002. The ANDA included a "Paragraph IV Certification" that the asserted patents were "invalid, or unenforceable, or will not be infringed" by the proposed generic. (PX 21 at FPC221273, FPC221283.) Further, ESI filed a patent application for its propofol formulation that included DTPA, which matured into U.S. Patent No. 6,028,108 ("the '108 patent") on February 22, 2000. (Defendant's Exhibit ("DX") 152.)

V. Comparison of the Asserted Claims to the Accused Formulation

AstraZeneca contends that Mayne's filing of ANDA No. 76-452 on its generic propofol composition infringes Claims 1-14, 16-32 and 34 of each asserted patent as well as

Claims 38 and 39 of the '520 patent. Each asserted claim includes "edetate." The parties principally disagree over whether Mayne's formulation contains the edetate recited in the claims. That is, the parties dispute whether the calcium trisodium DTPA in Mayne's generic propofol emulsion qualifies as the edetate in the asserted claims.

Claim 1 of the '520 patent is as follows:

> [a][5] A sterile pharmaceutical composition for parenteral administration which comprises
>
> > [b] an oil-in-water emulsion in which propofol dissolved in a water-immiscible solvent, is emulsified with water and stabilized by means of a surfactant,
> >
> > [c] and which further comprises an amount of edetate sufficient to prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours as measured by a test wherein a washed suspension of each said organism is added to a separate aliquot of said composition at approximately 50 colony forming units per ml, at a temperature in the range 20°-25° C., whereafter said aliquots are incubated at 20°-25° C. and are tested for viable counts of said organism after 24 hours,
> >
> > [d] said amount of edetate being no more than 0.1% by weight of said composition.

(PX 1, Col. 11, lines 32-48.) This Court previously construed three disputed claim terms as follows:

Claim Term	**Meaning**
"Edetate"	EDTA as well as compounds structurally related to EDTA regardless of how they are synthesized, and which can prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at

[5] Claim 1 has been subdivided into four subsections for ease of reference.

	least 24 hours.
"Propofol"	2,6-diisopropylphenol.
"an amount of edetate . . ."	An amount of edetate, greater than 0% but less than or equal to 0.1% by weight of the pharmaceutical composition, which is sufficient to meet the microbiological test recited in the claim phrase.

AstraZeneca, 352 F. Supp. 2d at 419.

A. Analysis for Literal Infringement

As discussed below, Mayne's generic propofol emulsion includes each limitation recited in Claims 1, 3-14 of each asserted patent and Claim 38 of the '520 patent.

1. Claims 1 and 3-14 of the '520 Patent

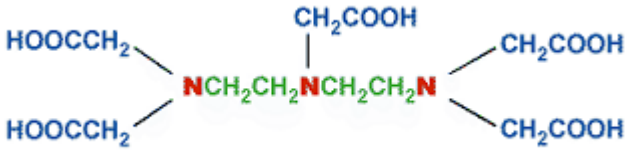
Limitation [a] of Claim 1 calls for "a sterile pharmaceutical composition for parenteral administration." Likewise, Mayne's generic propofol emulsion is also a sterile pharmaceutical composition for parenteral administration. (JPTO ¶¶ VI.B.8, 10; see also PX 21 at FPC221394, FPC221418.) Thus, the accused formulation meets this limitation.

Limitation [b] is "an oil-in-water emulsion in which propofol dissolved in a water-immiscible solvent, is emulsified with water and stabilized by means of a surfactant." As stipulated by the parties, Mayne's generic propofol emulsion is also an oil-in-water emulsion, which includes propofol at a concentration of 10 mg/ml (or 1% by weight) and soybean oil at a concentration of 100 mg/ml (or 10% by weight). The propofol is dissolved in soybean oil, which is emulsified with water and stabilized by a surfactant, egg lecithin. (JPTO ¶¶ VI.B.9, 11-13; see also PX 21 at FPC221292, FPC221394, FPC221418.) Thus, the accused formulation meets this limitation.

Limitation [c] is "an amount of edetate sufficient to [pass the recited microbiological test]." Mayne's formulation contains 0.0008% by weight of calcium trisodium DTPA. (JPTO ¶¶ VI.B.21-23.) As noted above, the calcium trisodium DTPA in Mayne's generic propofol emulsion passes the microbiological test recited in Claim 1. (JPTO ¶ VI.B.22.) Thus, the key question is whether the calcium trisodium DTPA in Mayne's formulation is structurally related to EDTA (i.e., whether it is an edetate).

The EDTA free acid structure may be depicted as follows:

(Tr. at 1063-64; see also Tr. at 1381-82.) The DTPA free acid structure may be illustrated as:



(Tr. at 1072; see also Tr. at 1381-82; PX 281 at FPC255811.) DTPA cannot "easily" be synthesized from EDTA in a laboratory (Tr. at 292-93); however, it can theoretically be synthesized from EDTA (Tr. at 284-86), because both DTPA and EDTA are members of a class of structurally analogous compounds known as polyaminopolycarboxylic acids (Tr. at 1363-65).

AstraZeneca's expert, Dr. Jack Norton,[6] testified on the topic of whether DTPA and EDTA are structurally related. (Tr. at 281-86.) Dr. Norton concluded that, based on his knowledge of the "chemical literature," DTPA and EDTA were structurally related. (Tr. at 285-88.) AstraZeneca's other expert, Thomas Foster,[7] also testified that DTPA and EDTA are structurally related. (Tr. at 156-59, 1297-98.) Similarly, Mayne's expert, Dr. Norman Weiner,[8] testified that "DTPA is a structural analog of EDTA." (Tr. at 869.) Although Mayne's other expert, Dr. Harold Hopfenberg,[9] resisted conceding that DTPA was structurally related to EDTA, he acknowledged that the two are structural analogs and belong to the same structurally

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[6] Dr. Norton has been a professor of chemistry at Columbia University since 1997, and has taught courses in organometallic chemistry, organic chemistry and kinetics. Dr. Norton has published approximately 130 articles in connection with his work and is a co-author of the textbook, "Principles and Applications of Organotransition Metal Chemistry." He has also been a recipient of various honors including a Sloan fellowship, a Dreyfus Foundation scholarship, a Guggenheim fellowship and fellowship from the Japan Society for the Promotion of Science, and has been awarded the Organometallic Chemistry Award by the American Chemical Society. (Tr. at 267-71; PX 330.)

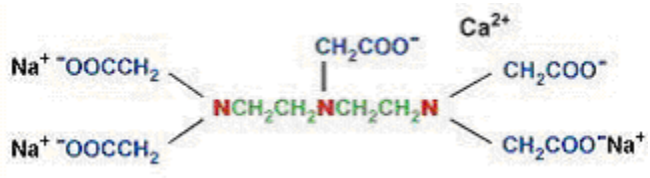
[7] Dr. Foster is a professor of pharmacy and anesthesiology in the College of Medicine at the University of Kentucky and teaches courses in the pharmaceutical sciences. Dr. Foster also serves as a special government employee with the FDA and has advised the FDA regarding biopharmaceutics and pharmacokinetics. He has been awarded fellowships by the American College of Clinical Pharmacology, American College of Clinical Pharmacy and the American Pharmaceutical Association, and has published over 100 papers. (Tr. at 119-25; PX 333.)

[8] Dr. Weiner was an Emeritus Professor of Pharmaceutics at the University of Michigan in Ann Arbor. (Tr. at 673.) His main area of research includes liquid formulations involving liposome emulsions which depend on the presence of phosphatides and lecithin. He has published approximately 175 research papers primarily in this area and has taught a course to the pharmaceutical and cosmetic industries in emulsions and suspensions for twenty-five years. (Tr. at 677.) Finally, Dr. Weiner helped Pharmcia Company develop its 10%, 20% and 30% oil Intralipid products. (Tr. at 679-80.)

[9] Dr. Hopfenberg is the Camille Dreyfus Professor Emeritus of chemical engineering at North Carolina State University. His professional career has focused on chemistry, applied chemistry and product development. He is also a longtime consultant for the Alza Corporation, a world leader in the development of controlled and sustained drug delivery systems in pharmaceutical formulations. (Tr. at 1043-55; DX 183.)

analogous polyaminopolycarboxylic acid family of compounds. (Tr. at 1363-64.) Thus, as compounds in the same family of chemical structures, this Court finds that DTPA is a structural analog of EDTA. Further, as this Court stated in its Markman ruling, "the proper definition of edetate includes EDTA as well as . . . structural analogs of EDTA." AstraZeneca, 352 F. Supp. 2d at 417. That is, as EDTA's structural analog, DTPA is structurally related to EDTA and is an edetate as that term is used in Claim 1. See AstraZeneca, 352 F. Supp. 2d at 417. That does not end the inquiry, however, because the compound in Mayne's formulation is calcium trisodium DTPA – not DTPA.

Calcium trisodium DTPA may be depicted as follows:



(See Tr. at 863, 865-66.) As this depiction illustrates, calcium trisodium DTPA contains the following chemical groups: ethylene (CH_2CH_2), amino (N) and carboxylic acid (also called acetic acid) (CH_2COO^-). In particular, calcium trisodium DTPA contains two ethylene, three amino and five carboxylic acid groups. Dr. Weiner testified that calcium trisodium DTPA is a salt of DTPA. (Tr. at 863.) Because calcium trisodium DTPA is a salt instead of an acid, it includes one calcium ion and three sodium ions instead of the four hydrogen ions present in DTPA. (Tr. at 856-66, 1299-1301, 1359-61; PX 281 at FPC255811; PX 437-2.) Dr. Hopfenberg testified that all salts of DTPA have the basic structure of DTPA. (Tr. at 1361.) Thus, calcium trisodium DTPA has the basic structure of DTPA. (Tr. at 863, 865-66, 1361; PX 281 at FPC255811.) Moreover, as a salt of DTPA, this Court finds that calcium trisodium DTPA is a derivative of DTPA. (Tr. at 860-61; DX 152, Col. 2, lines 1-5 (Mayne's patent stating that calcium trisodium DTPA is a derivative of DTPA).)

Finally, because calcium trisodium DTPA is structurally related to DTPA (i.e., calcium trisodium DTPA is a derivative of DTPA), it is structurally related to EDTA. (Tr. at 156-59 (discussing the calcium trisodium DTPA additive in Mayne's generic propofol emulsion, although imprecisely referring to it simply as DTPA); JX 4 (noting that calcium trisodium DTPA is "structurally similar to edetate"); PX 437-2; see Tr. at 944, 1297-1302; PX 21 at FPC221291-96 (Mayne's ANDA submission discussing the similarities between calcium trisodium DTPA and EDTA).) In fact, calcium trisodium DTPA is a member of the polyaminocarboxylic family, like EDTA and DTPA. (Tr. at 1300-01; PX 437-2; see Tr. at 856-66, 1299-1301, 1359-61; PX 281 at FPC255811; PX 437-1; PX 437-2.) As members of the same family, calcium trisodium DTPA and EDTA are structurally related (i.e., calcium trisodium DTPA is a derivative of EDTA). (See Tr. at 1363-64). See AstraZeneca, 352 F. Supp. 2d at 417. Thus, this Court finds that the accused formulation meets limitation [c].

Limitation [d] of Claim 1 requires that the edetate be no more than 0.1% by weight of the composition. Because the amount of calcium trisodium DTPA in Mayne's generic propofol formulation, 0.0008% by weight, is less than 0.1% by weight of the formulation, Mayne's composition meets this limitation. (JPTO ¶¶ VI.B.21, 23; see Tr. at 159; PX 433-3.)

Claims 3-14 of the '520 patent depend on Claim 1, thereby incorporating all the limitations of Claim 1. Claims 3-14 add further limitations relating to various attributes of the components of the claimed compositions other than the disputed "edetate" limitation. Because Mayne's formulation includes these additional limitations (JPTO ¶¶ VI.B.11-13,15-19; see Tr. at 160-64; PX 433-4 – 433-15), the accused formulation meets all the limitations in Claims 3-14 of the '520 patent.

2. Claim 38 of the '520 Patent

Independent Claim 38 of the '520 patent is identical to Claim 1, but adds that "the edetate does not physically destabilise [the] emulsion." Similarly, calcium trisodium DTPA does not destabilize Mayne's generic propofol formulation. (Tr. 164-66; PXs 433-16, 433-17, 433-18; see Tr. 952-53; JX 12 at FPC205490; PX 21 at FPC221415-16, FPC221418-19.) Thus, Mayne's formulation meets all the limitations in Claim 38 of the '520 patent.

3. Claims 1 and 3-14 of the '355 and '356 Patents

Claim 1 of both the '355 and the '356 patents are method claims. Claim 1 of the '355 patent is directed to a method for "producing anaesthesia in a warm-blooded animal which comprises parenterally administering" a propofol and edetate oil-in-water emulsion. (PX 2, Col. 11, lines 36-53.) Claim 1 of the '356 patent is directed to a method for "limiting the potential for microbial growth" in a propofol oil-in-water emulsion with edetate. (PX 3, Col. 11, lines 32-49.) The practice of Mayne's generic propofol formulation will read on these claimed methods. (JPTO ¶¶ VI.B.8, 20-23; Tr. at 134-35, 167-69, 173-75; PX 21 at FPC221292, FPC221296, FPC221391, FPC221394-95, FPC221437; PX 35 at FPC221547-48, FPC221559, FPC221573; PX 281 at FPC255829; PX 433-19–433-21, 433-34–433-35.)

Claims 3-14 of the '355 and '356 patents depend on Claim 1 of their respective patents. These dependent claims add limitations to components of the patented formulations other than the disputed "edetate." Mayne's proposed formulation includes these additional limitations. (JPTO ¶¶ VI.B.8, 20-23; Tr. at 169-73, 175-78; PX 433-22–433-33, 433-36–433-47.)

B. Analysis Under the Doctrine of Equivalents

As discussed below, Mayne's generic propofol emulsion includes each limitation recited in Claims 1-14, 16-32 and 34 of each asserted patent as well as Claims 38 and 39 of the '520 patent when viewed under the rubric of the doctrine of equivalents. In particular, calcium trisodium DTPA and EDTA salts[10] perform the same function in substantially the same way to achieve the same result.

The edetate in the asserted claims retards microbial growth in propofol oil-in-water emulsions. As already noted, calcium trisodium DTPA in Mayne's generic propofol formulation has the same function. (JPTO ¶¶ VI.B.21-23; see also PX 21 at FPC221296 (noting that the DTPA in Mayne's generic propofol formulation is "considered to behave in a similar manner to EDTA, the microbial inhibitor contained in the brand product Diprivan at 0.005%"); DX 152, Col. 1, line 60 – Col. 2, line 5.) Thus, this Court finds that calcium trisodium DTPA performs the same function as the edetate in the asserted claims.

EDTA salts, such as disodium edetate, and calcium trisodium DTPA are both metal ion chelators. (Tr. at 867-68, 887-88; see Tr. at 272.) EDTA salts perform their antimicrobial function by chelating the metal ions that microorganisms need to grow. (See Tr. at 272, 867-68 (noting that the salts of EDTA are metal ion chelators), 939-40; 1212-15.) Similarly, calcium trisodium DTPA performs its antimicrobial function by chelation. (Tr. at 867-69 (noting that the salts of DTPA are metal ion chelators); see 1209-12; DX 62 at FPC255346; PX 99 at FPC067907 ("The mechanism of EDTA as an antibacterial is that it complexes the metal ions essential for bacteria to survive.").)

[10] EDTA salts are derivatives of EDTA and, therefore, are edetates.

At trial, AstraZeneca's expert, Dr. Joseph E. Knapp,[11] testified that the microorganisms that thrive in propofol oil-in-water emulsions all require metal ions to grow. (Tr. at 308-12, 320-27; JX 29 at AZ100715-16, AZ100722, AZ100730; see Tr. at 1209-13; DX 65 at FPC252691-92.) Indeed, in July 2003, the FDA sent Mayne a "deficiency letter" in connection with its ANDA,[12] requesting information about the safety of calcium trisodium DTPA in Mayne's generic propofol formulation. In response, Mayne submitted an expert report by Dr. John W. Kille.[13] The Kille report explains that calcium trisodium DTPA "is effective [as a microbial inhibitor] as a result of its ability to chelate divalent metal ions that are essential for many biological processes." (PX 281 at FPC255829.) In light of Dr. Knapp's testimony, Dr. George's memorandum (JX 4) and Mayne's statements to the FDA (PX 281 at FPC255829), this Court finds that calcium trisodium DTPA performs in the same manner as EDTA salts, i.e., the edetate in the asserted claims.

Finally, the edetate in the asserted claims retards microbial growth to the extent required by the microbiological test set forth in the claims. Mayne's calcium trisodium DTPA achieves the same result. (JPTO ¶¶ VI.B.21-23; Tr. at 473, 1205-06.) Thus, this Court finds that calcium trisodium DTPA achieves the same result as the edetate in the asserted claims, and is equivalent to the edetate in the asserted claims. Further, as discussed above, Mayne's generic

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[11] Dr. Knapp has thirty-four years of experience as a professor of Pharmaceutical Science at the University of Pittsburgh School of Pharmacy. He is an advisor to the FDA on issues of microbiology, has six patents under his name and is the author of over seventy peer-reviewed articles and book chapters. (Tr. at 300-04; PX 331.)

[12] A deficiency letter is a request for additional information from the FDA.

[13] Mayne objects to the Kille report as a statement by "an independent contractor, not affiliated with Mayne." (Mayne's Response to AstraZeneca's Proposed Findings of Fact and Conclusions of Law, dated Apr. 18, 2005 ("Mayne Opp.") at 6-7.) This objection is overruled. By submitting the Kille report to the FDA as part of its response, Mayne adopted that report's contents as its own. Therefore, the Kille report is admissible as Mayne's admission against interest.

propofol formulation includes the other limitations of Claims 1 and 3-14 of the asserted patents and Claim 38 of the '520 patent.

Claims 16-19 of the asserted patents and Claim 39 of the '520 patent describe the amount of edetate present in the claimed composition. The claims specify molar concentrations of edetate of $3x10^{-5}$ to $9x10^{-4}$, $3x10^{-5}$ to $7.5x10^{-4}$, $1.5x10^{-4}$ to $3x10^{-4}$ and $1.5x10^{-4}$, respectively. Because calcium trisodium DTPA is 0.0008% by weight in Mayne's generic propofol formulation, that constitutes a molar concentration of $2x10^{-5}$. (JPTO ¶¶ VI.B.21-23.) This Court finds that a molar concentration of $2x10^{-5}$ is equivalent to the molar concentrations of edetate recited in these claims. Additionally, as discussed above, the calcium trisodium DTPA in Mayne's formulation acts as an antimicrobial agent to perform the same function in the same way (i.e., chelation) and achieves the same result (i.e., passing the microbiological test) as the edetate in the asserted claims. (see JPTO ¶¶ VI.B.21-23.) Finally, as noted above, Mayne's generic propofol formulation includes the other limitations of Claims 16-19 of the asserted patents and Claim 39 of the '520 patent.

Claims 21-32 of the asserted patents depend, directly or indirectly, on one or more of Claims 16-19, but add further limitations. Mayne's generic propofol emulsion includes these additional limitations. (Tr. at 188-92, 220-23, 232-35; PX 434-22–434-33, 434-61–434-72, 434-94–434-105.)

Claims 2 and 20 of the AstraZeneca patents depend on Claims 1 and 16-19, respectively, and specify the edetate as disodium edetate. Claim 34 of the asserted patents specifies that the claimed formulation contains 0.005% by weight disodium edetate. This Court finds that the amount of calcium trisodium DTPA is equivalent to that of disodium edetate in the asserted claims. Further, as with edetate, calcium trisodium DTPA satisfies the function-way-

result test because it performs the same function in the same way to achieve the same result as the disodium edetate in the claims. Mayne's formulation includes the other limitations of Claims 2, 20 and 34 of the asserted patents. (Tr. at 188, 192-94, 207, 213, 219-20, 223-24, 226, 232, 235-36; PX 434-4, 434-21, 434-34, 434-42, 434-60, 434-73, 434-76, 434-93, 434-106.)

VI. Prior Art

A. The Glen Patents

Mayne contends that the asserted claims are anticipated or rendered obvious by the disclosures in UK patent No. 1,472,793 ("Glen UK patent"). The Glen UK patent discloses the anesthetic properties of propofol as well as methods of making a propofol formulation. U.S. Patent No. 4,056,635 (the "Glen '635 patent") is the U.S. counterpart to the Glen UK patent and has the same specification. (Compare DX 177 at AZ033340-47, with DX 177 at AZ033257-62.) The Glen patents are mentioned in the specification of the asserted patents and were discussed during prosecution. Indeed, the Glen patents were the principal references in the Patent Examiner's office actions. (Tr. at 780, 832-38; DX 177 at AZ033245-52, AZ033257-62, AZ033340-47, AZ033502-05; DX 178 at AZ033536-39, AZ033780-83; PX 1 at Cover, Col. 1, line 32 - Col. 4, line 37.)

The Glen UK patent discloses a propofol composition, together with any of over a dozen classes of suitable solvents or solubilizing agents (used alone or in combination) and, in the case of an emulsion, one of over a dozen types of suitable surfactants to stabilize the emulsion. In addition, the Glen UK patent mentions five broad classes of constituents that may be added to the disclosed formulations: "stabilizers, preservatives, antioxidants, metal ion sequestering agents and antifoaming agents." (Tr. at 815-16.) The Glen UK patent also provides

twenty-three exemplary compositions. Two of those compositions (Examples 2 and 3) describe the use of sodium edetate as a metal ion sequestering agent. (Tr. at 815-17, 830-32; DX 177 at AZ033340-42.) These examples do not disclose propofol dissolved in a water-immiscible solvent. (Tr. at 810.) Additionally, these two embodiments are not oil-in-water emulsions, but micro-emulsions that use substantially smaller droplets than a conventional oil-and-water emulsion. A micro-emulsion is thermodynamically stable (i.e., it does not tend to separate over time), while a conventional emulsion is thermodynamically unstable. This is an important difference because at the time of the invention covered by the asserted patents, it was believed that additives should be avoided in oil-in-water emulsions because they destabilize the emulsion. (Tr. at 788-89, 803-06, 810-11, 813-14, 889-91; DX 177 at AZ033342.)

Indeed, the Glen UK patent does not discuss microbial contamination or suggest adding edetate to an oil-in-water emulsion to retard microbial growth. In this regard, the Glen UK patent does not suggest any test to determine whether growth had been sufficiently retarded as claimed in the '520 patent, or the methods of the '355 and '356 patents. Indeed, in issuing the asserted patents, the USPTO concluded that the Glen UK patent did not teach the inventions of the asserted patents.

B. Other Prior Art

In addition to the above, other relevant prior art references include articles by J. Roger Hart. See J. Roger Hart et al., Chelating Agents As Preservative Potentiators, Cosmetic and Drug Preservation: Principles and Practice 323-37 (PX 178 at AZ027037-40); J. Roger Hart, EDTA-Type Chelating Agents in Personal Care Products, Cosmetics and Toiletries 54 (Apr. 1983) (DX 178 at AZ033667-71.) The two articles refer to the use of EDTA and related

derivatives, such as DTPA, as antimicrobial agents against Pseudomonas aeruginosa. The articles note that EDTA may potentiate (i.e., boost) the effect of other antimicrobial agents such as phenolic compounds, and set forth lists of preservatives known to be enhanced by EDTA, including phenolic compounds. The articles do not, however, disclose that EDTA is an effective broad-spectrum antimicrobial agent. (Tr. at 840-45.) Nor do they teach how to use EDTA with propofol in an oil-in-water emulsion to satisfy the microbiological test recited in the asserted claims. Another article, R. P. Patel & A. B. Shah, Disodium Salt of EDTA As An Antimicrobial Agent, The Indian Journal of Pharmacy (May 1965) (the "Patel reference") (DX 4), teaches that disodium EDTA may be effective as a broad-spectrum antimicrobial agent when used at a concentration of 2% ─ much higher than those in the asserted patents. (Tr. at 758-59, 1149.)

Another pertinent article in the prior art is B. P. Chew et al., In Vitro Growth Inhibition of Mastitis Causing Bacteria by Phenolics and Metal Chelators, J. Dairy Sci. 68:3037 (1985) (DX 177 at AZ033396-405) (the "Chew article"). The Chew article addresses the treatment of cow udder infections with antimicrobial agents such as EDTA and DTPA. The article further discloses that EDTA is bactericidal against gram-positive bacteria, but relatively ineffective against gram-negative bacteria such as Escherichia coli. According to this article, DTPA is less effective than EDTA against gram-positive bacteria, but more effective than EDTA against gram-negative bacteria. (DX 177 at AZ033396-405.)

At trial, Mayne elicited testimony regarding U.S. Patent No. 3,240,701 (the "'701 patent"), issued to Thomas E. Furia. (DX 61, Col. 1, line 9 - Col. 2, line 39.) The '701 patent is directed to the problem of sludge formation caused by microbes in industrial fluids, such as jet fuel, cutting fluids and injection systems for oil recovery, and does not relate to anesthetic compositions for administration to warm-blooded animals. (Tr. at 846-48, 1207.)

Finally, at trial, there was testimony regarding internal unpublished work by AstraZeneca on high-propofol and low-oil emulsions. (Tr. at 1002.) These experiments, performed after the inventors had conceived the use of edetate to retard microbial growth, related to formulations that prevented microbial growth without an antimicrobial additive. Further, this confidential and unpublished work was performed in the United Kingdom, not offered for sale and involved the inventors of the asserted patents or the inventors' co-workers. This work was later abandoned by AstraZeneca because that formulation caused excessive pain on injection and raised issues of patient safety and formulation instability. (Tr. at 1002, 1021-22; see also Tr. at 737-38.)

VII. Prior Art Cited During Prosecution History

During the prosecution of the '520 patent, the applicants made five separate Information Disclosure Statement ("IDS") submissions to the USPTO (Tr. at 569-76; DX 177 at AZ033245-52, AZ033415-17, AZ033446-48, AZ033523-25; DX 178 at AZ033578-81), citing, what Jules Goldberg[14] testified was, a "huge amount of art." (Tr. at 538.) Goldberg concluded that "the patentees . . . had dug up just about [every prior art] they could." (Tr. at 538.) The cited art includes the Glen UK patent, the Glen '635 patent and the Original Diprivan formulation, all of which appear in the '520 patent's specification.

The patent specification states that propofol is a phenol. The prior art cited by the inventors discloses that phenols have antimicrobial properties. In particular, the Hart articles and an article by Jon J. Kabara disclose that phenols are antimicrobial agents and that EDTA was

[14] Mr. Goldberg, a partner at Reed Smith LLP, has been a patent attorney for over thirty years in the chemical and pharmaceutical arts. (Tr. at 520-26.) He is Mayne's litigation counsel in this action.

known to potentiate the antimicrobial properties of such phenols. (Tr. at 778-80, 840-45; PX 178 at AZ027032, AZ027037; DX 178 at AZ033668-69, AZ033677-85; see Tr. at 1149-54; JX 18 at FPC217835-837; JX 22 at FPC254665-67.) Indeed, after her review of the '520 patent, ESI's Dr. George acknowledged the antimicrobial properties of propofol. (Tr. at 939-40; PX 99 at FPC067907 ("Since propofol itself is a phenol, its antibacterial action is potentiated by the addition of a chelating agent, such as EDTA.").) Mayne contends that the antimicrobial properties of propofol were not known "by anyone outside of AstraZeneca at the time of the prosecution of the patents in suit." (See Mayne's Proposed Findings of Fact and Conclusions of Law, dated Apr. 8, 2005 ("Mayne Mem.") at 35 ("AstraZeneca failed to produce any evidence to show that information regarding propofol's antimicrobial properties . . . was published or otherwise known by anyone outside of AstraZeneca at the time of the prosecution of the Patents in Suit.").) However, the prior art references demonstrate that the patentees did not conceal propofol's antimicrobial properties.

VIII. Mayne's Pre-Litigation Conduct

ESI designed its generic propofol formulation to parallel the qualities of Original Diprivan. Upon learning of the '520 patent, ESI selected calcium trisodium DTPA, in part, because Dr. George believed that it did not infringe the '520 patent. (Tr. at 944-47; JX 4.)

In the summer of 2000, Wyeth asked Paul Heller,[15] a partner in the intellectual property law firm of Kenyon & Kenyon, for advice on whether its proposed formulation would infringe the asserted patents. (Tr. at 1108-11.) Heller delivered a written opinion that the proposed propofol formulation would not infringe AstraZeneca's patents literally or under the

[15] Mr. Heller was a patent attorney for over thirty years, concentrating primarily in the chemical and pharmaceutical fields. (Tr. at 1108-09.) He died of injuries sustained in a bicycle accident.

doctrine of equivalents. (Tr. at 1111-13; JX 18.) While Heller did not "consider[] in depth the issue of whether the '520 patent [was] valid," he intimated that patentees' "arguments for patentability as asserted to the USPTO would fail" in a lawsuit. (JX 18 at FPC217866.) In 2002, Thomas Meloro,[16] a partner at Kenyon & Kenyon, updated the 2000 opinion. (Tr. at 1108; JX 21.) Meloro agreed with Heller's analysis and conclusion that there was no literal infringement or infringement under the doctrine of equivalents. (JX 21.)

Meloro subsequently assisted in preparing Wyeth's August 20, 2002 notice to AstraZeneca that it intended to file an ANDA. (Tr. 1134-36.) The notification letter stated that the asserted patents were "invalid, unenforceable, or not infringed, either literally or under the doctrine of equivalents" by the importation into, or manufacture, use, sale or offer for sale in the United States of Wyeth's generic propofol emulsion. (PX 121 at FPC207044, FPC207063.)

Thereafter, in August 2002, Baxter (i.e., Wyeth's successor) offered to sell its rights to the propofol formulation to Mayne. (Tr. at 463.) Mayne undertook due diligence with respect to the proposed asset purchase (Tr. at 613-18), and retained Goldberg to provide a due diligence opinion (Tr. at 474-76). In a written opinion, Goldberg concluded that the product described in the ANDA did not infringe the asserted patents, literally or under the doctrine of equivalents. (Tr. at 547-48; JX 25.) However, he noted that "[t]he [AstraZeneca] patents are valid and enforceable" and that suggestions to the contrary in the Kenyon & Kenyon opinions were "weak at best." (Tr. at 535-37, 587-89; Tr. 667-68; JX 25 at FPC251527, FPC251529; see JX 26 at FPC252289, FPC252292, FPC2522294; JX 27 at FPC252274, FPC252276.) Goldberg concluded that "the [patentee's] arguments [to the USPTO] were legitimate," and that the modified claims were sufficiently distinguished from the cited art. (JX 26 at FPC252294.) He

[16] Mr. Meloro is a patent attorney, concentrating in pharmaceutical and biotechnology matters. (Tr. at 1104-07.)

further noted that "a properly informed Court would find this cited art insufficient to invalidate the claims." (JX 25 at FPC251527-29; see Tr. at 537-39.)

In 2003, Mayne obtained another opinion from Meloro for an amendment to its ANDA. After reviewing the relevant information, Meloro again opined that the formulation would not infringe any of the AstraZeneca patents. (Tr. at 1139; JX 22 at FPC254700.) In July 2003, Mayne filed the amendment to its ANDA and sent a notification letter to AstraZeneca. (Tr. at 496; PX 123; JX 22 at FPC254660 n.1.) The notification letter concluded that the asserted patents were invalid, unenforceable and not infringed by Mayne's propofol product. (Tr. at 500-01.)

CONCLUSIONS OF LAW

I. ANDA Litigation

Filing an ANDA to "obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . claimed in a patent or the use of which is claimed in a patent before [its] expiration" constitutes patent infringement. Teva Pharms. USA, Inc. v. Pfizer Inc., 395 F.3d 1324, 1328 (Fed. Cir. 2005). Indeed, "35 U.S.C. § 271(e)(2)(A) simply provides an 'artificial' act of infringement that creates case-or-controversy jurisdiction to enable the resolution of an infringement dispute before the ANDA applicant has actually made or marketed the proposed product." Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365 (Fed. Cir. 2003) (citing Glaxo Inc. v. Novopharm Ltd., 110 F.3d 1562, 1569 (Fed. Cir. 1997)).

"Once jurisdiction is established, however, the substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits, including those in a non-

ANDA context, the only difference being that the inquiries now are hypothetical because the allegedly infringing product has not yet been marketed." Warner-Lambert, 316 F.3d at 1365. "The plain language of 35 U.S.C. § 271(e)(2)(A) does not alter a patentee's burden of proving infringement." Warner-Lambert, 316 F.3d at 1366 (internal quotation and alterations omitted). "The proper inquiry under § 271(e)(2)(A) is 'whether, if a particular drug were put on the market, it would infringe the relevant patent.'" Warner-Lambert, 316 F.3d at 1366 (quoting Bristol-Myers Squibb Co. v. Royce Labs., Inc., 69 F.3d 1130, 1135 (Fed. Cir. 1995). Thus, this Court's infringement inquiry must focus on Mayne's ANDA. See Glaxo, 110 F.3d at 1569.

II. Markman Ruling

Claim construction is an issue of law to be resolved by the Court. Markman v. Westview Instruments, Inc., 517 U.S. 370, 388-90 (1996). On December 28, 2004, the Court issued a Memorandum and Order construing three disputed claim terms of the patents in suit.

As already noted, this Court construed the claim term "edetate" as "EDTA as well as compounds structurally related to EDTA regardless of how they are synthesized, and which can prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours." AstraZeneca, 352 F. Supp. 2d at 419. Mayne argues that this Court's definition is contrary to the holding of Phillips v. AWH Corp., 415 F.3d 1303 (Fed. Cir. 2005), because it overemphasized the dictionary definition of edetate and minimized the weight accorded to the asserted patents' specification and prosecution history. (Letter to Court from Jules Goldberg, dated Aug. 4, 2005 at 1-3; Letter to Court from Jules Goldberg, dated July 15, 2005 at 1-2.) This Court disagrees.

In Phillips, the Federal Circuit noted:

> The main problem with elevating the dictionary to such prominence is that it focuses the inquiry on the abstract meaning of words rather than on the meaning of claim terms within the context of the patent.
>
> * * *
>
> Dictionaries, by their nature, provide an expansive array of definitions. General dictionaries, in particular, strive to collect all uses of particular words, from the common to the obscure. By design, general dictionaries collect the definitions of a term as used not only in a particular art field, but in many different settings. In such circumstances, it is inevitable that the multiple dictionary definitions for a term will extend beyond the "construction of the patent [that] is confirmed by the avowed understanding of the patentee, expressed by him, or on his behalf, when his application for the original patent was pending." Goodyear Dental Vulcanite Co. v. Davis, 102 U.S. 222, 227 (1880). . . .
>
> Even technical dictionaries or treatises, under certain circumstances, may suffer from some of these deficiencies. There is no guarantee that a term is used in the same way in a treatise as it would be by the patentee. In fact, discrepancies between the patent and treatises are apt to be common because the patent by its nature describes something novel. . . .
>
> Moreover, different dictionaries may contain somewhat different sets of definitions for the same words. A claim should not rise or fall based upon the preferences of a particular dictionary editor, or the court's independent decision, uninformed by the specification, to rely on one dictionary rather than another. Finally, the authors of dictionaries or treatises may simplify ideas to communicate them most effectively to the public and may thus choose a meaning that is not pertinent to the understanding of particular claim language. . . . The resulting definitions therefore do not necessarily reflect the inventor's goal of distinctly setting forth his invention as a person of ordinary skill in that particular art would understand it.

415 F.3d at 1321-22.

Thus, while the Federal Circuit did not "preclude the appropriate use of dictionaries," Phillips, 415 F.3d at 1322, it noted that the analysis should begin by giving claim

terms their ordinary and customary meaning as the terms would have been construed by "a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." Phillips, 415 F.3d at 1312-13. However, "[b]ecause the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean." Phillips, 415 F.3d at 1314 (internal quotations omitted). "Those sources include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." Phillips, 415 F.3d at 1314 (internal quotations omitted).

Finally, the Federal Circuit noted that "there is no magic formula or catechism for conducting claim construction" and that "[t]he sequence of steps used by the judge in consulting various sources is not important; what matters is for the court to attach the appropriate weight to be assigned to those sources in light of the statutes and policies that inform patent law." Phillips, 415 F.3d at 1324. The Federal Circuit rejected the approach it previously suggested in Texas Digital Systems, Inc. v. Telegenix, Inc., 308 F.3d 1193 (Fed. Cir. 2002), which overemphasized the weight afforded to dictionary definitions and minimized the weight afforded to a patent's specification and prosecution history. Phillips, 415 F.3d at 1320-24. However, as noted, the court did not bar the use of general purpose or technical dictionaries. Phillips, 415 F.3d at 1322.

This Court's claim construction was consistent with the approach suggested in Phillips. In its Markman ruling, this Court started its inquiry by attempting to decipher the meaning the patentees accorded to the disputed terms because "[t]he parties [did] not dispute that

the patentees manifested their intent to act as their own lexicographers in defining edetate." AstraZeneca, 352 F. Supp. 2d at 412; see also Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996) ("Although words in a claim are generally given their ordinary and customary meaning, a patentee may choose to be his own lexicographer and use terms in a manner other than their ordinary meaning, as long as the special definition of the term is clearly stated in the patent specification or file history.").

This Court found that the patentees had defined "edetate" in the specification. AstraZeneca, 352 F. Supp. 2d at 412. However, the Court rejected limiting the term "edetate" to the examples provided in the specification because the specification's phraseology "ma[de] it clear that patentees were merely providing illustrations." AstraZeneca, 352 F. Supp. 2d at 414; see also Phillips, 415 F.3d at 1327 ("We have held that the fact that a patent asserts that an invention achieves several objectives does not require that each of the claims be construed as limited to structures that are capable of achieving all of the objectives." (internal quotations and alterations omitted)).

While the specification defines edetate as "EDTA and derivatives thereof," Mayne argued that the term "derivatives" was limited to "synthetic derivatives only." AstraZeneca, 352 F. Supp. 2d at 414. To assist in its claim construction, this Court consulted the general purpose and technical dictionaries cited during the briefing, but found that "[t]he cacophony of dictionary definitions cited by the parties does not aid this Court's analysis of whether either [party's proposed] definition is conclusively established." AstraZeneca, 352 F. Supp. 2d at 416. As a result, "this Court . . . examine[d] the specification and the prosecution history to determine which definition or definitions are consistent with the spirit of the claimed invention." AstraZeneca, 352 F. Supp. 2d at 416. Based on the specification, this Court noted:

> The '520 patent teaches that disodium edetate, trisodium edetate, tetrasodium edetate and disodium calcium edetate are appropriate EDTA derivatives. (Col. 4, lines 51-57.) However, the '520 patent notes that the exact type of edetate is not important, as long as the chosen edetate can prevent significant growth of microorganisms for at least twenty-four hours if there is adventitious extrinsic contamination. (Col. 4, lines 57-64.) Thus, the specification supports a broad definition of edetate: EDTA or an EDTA derivative that can prevent significant growth of microorganisms for at least twenty-four hours.

AstraZeneca, 352 F. Supp. 2d at 416. This Court rejected Mayne's proposal to narrow the definition to synthetic derivatives only because "the patentees did not disavow structural analogs from their definition of derivatives or criticize their usage. Instead, . . . the patentees' use of the word derivatives suggests that they intend their definition to incorporate compounds that are similar in structure to the parent compound." AstraZeneca, 352 F. Supp. 2d at 417; see also Phillips, 415 F.3d at 1325-27 (rejecting a limiting definition of "baffles").

As the above recitation illustrates, in construing the claim with respect to the term "edetate," this Court consulted various sources but gave primacy to the claims and the specification. Thus, this Court's analysis conformed to the rule announced in Phillips.

III. Infringement

AstraZeneca, as the plaintiff in this action, bears the burden of proving infringement by a preponderance of the evidence. SmithKline Diagnostics, Inc. v. Helena Labs. Corp., 859 F.2d 878, 889 (Fed. Cir. 1988). Infringement analysis requires applying the asserted claims to the accused products and methods. Allen Eng'g Corp. v. Bartell Indus., Inc., 299 F.3d 1336, 1351 (Fed. Cir. 2002) ("Infringement is determined by comparing the accused devices not with products made by the patentee but with the claims of the patent as properly construed."). Where the filing of an ANDA triggers a patent infringement suit, the infringement analysis

requires comparison of the asserted claims to the product that is likely to be sold following FDA approval. Abbott Labs. v. TorPharm, Inc., 300 F.3d 1367, 1373 (Fed. Cir. 2002).

A. Literal Infringement

1. General Principles

"Literal infringement requires that each and every limitation set forth in a claim appear in an accused product." Franks Casing Crew & Rental Tools, Inc. v. Weatherford Int'l, Inc., 389 F.3d 1370, 1378 (Fed. Cir. 2004) (internal citation omitted); Amhill Enters., Ltd. v. Wawa, 81 F.3d 1554, 1562 (Fed. Cir. 1996) ("Literal infringement of a claim exists when every limitation recited in the claim is found in the accused device, i.e., when the properly construed claim reads on the accused device exactly."); Baxter Healthcare Corp. v. Spectramed, Inc., 49 F.3d 1575, 1582 (Fed. Cir. 1995). "If even one limitation is missing or not met as claimed, there is no literal infringement." Mas-Hamilton Group v. LaGard, Inc., 156 F.3d 1206, 1211 (Fed. Cir. 1998) (citations omitted). Further, "[i]t is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to have been infringed." Wahpeton Canvas Co. v. Frontier, Inc., 870 F.2d 1546, 1553 (Fed. Cir. 1989).

2. Application

Here, the accused product is Mayne's generic propofol formulation that is the subject of ANDA No. 76-452. As discussed above, with respect to Claims 1 and 3-14 of the asserted patents as well as Claim 38 of the '520 patent the only dispute is whether calcium trisodium DTPA qualifies as the edetate in the asserted claims. As used in the asserted patents, "edetate" means

> EDTA as well as compounds structurally related to EDTA regardless of how they are synthesized, and which can prevent a no more than 10-fold increase in growth of each of Staphylococcus aureus ATCC 6538, Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 10231 for at least 24 hours.

AstraZeneca, 352 F. Supp. 2d at 419. The claims require that edetate be present in an amount "greater than 0% but less than or equal to 0.1% by weight of the pharmaceutical composition, which is sufficient to meet the microbiological test recited in the claim phrase." AstraZeneca, 352 F. Supp. 2d at 419. Because, as discussed supra, Mayne's generic propofol formulation's calcium trisodium DTPA is an edetate, the accused product includes all the limitations in Claims 1, 3-14 and 38 of the '520 patent, Claims 1 and 3-14 of the '355 patent and Claims 1 and 3-14 of the '356 patent. Accordingly, this Court concludes that Mayne's generic propofol emulsion literally infringes Claims 1 and 3-14 of the asserted patents as well as Claim 38 of the '520 patent. See Baxter Healthcare, 49 F.3d at 1582 (holding that an accused product or method literally infringes when it includes every limitation of the asserted claim).

B. Infringement under the Doctrine of Equivalents

1. General Principles

"The doctrine of equivalents, ubiquitous since its origin in Winans v. Denmead, 56 U.S. (15 How.) 330 (1853), exists solely for the equitable purpose of preventing an infringer from stealing the benefit of an invention." Texas Instruments, Inc. v. U.S. Int'l Trade Com'n, 805 F.2d 1558, 1572 (Fed. Cir. 1986) (internal quotations omitted); see Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 339 U.S. 605, 608 (1950) (noting that the doctrine of equivalents serves "'[t]o temper unsparing logic and prevent an infringer from stealing the benefit of the invention.'" (quoting Royal Typewriter Co. v. Remington Rand, Inc., 168 F.2d 691, 692 (2d Cir. 1948)

(Hand, J.))). Where "one or more of the claim limitations are not literally present in the accused device, thus precluding a finding of literal infringement, the claim may still be held infringed if equivalents of those limitations are present." Allen Eng'g Corp. v. Bartell Indus., Inc., 299 F.3d 1336, 1345 (Fed. Cir. 2002) (citing Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 24 (1997)). The doctrine strikes a balance between ensuring that the patentee enjoys the full benefit of his patent and that the claims give "fair notice" of the patent's scope. London v. Carson Pirie Scott & Co., 946 F.2d 1534, 1538 (Fed. Cir. 1991).

Equivalents are assessed limitation-by-limitation. Warner-Jenkinson, 520 U.S. at 29, 40. For there to be infringement under the doctrine of equivalents, the differences between the absent claim limitations and accused product must be "insubstantial." Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp., 320 F.3d 1339, 1351 (Fed. Cir. 2003). "While no particular linguistic framework controls the inquiry, the insubstantial differences inquiry may be guided by determining whether the element in the accused device 'performs substantially the same function in substantially the same way to obtain the same result' as the claim limitation." Boehringer, 320 F.3d at 1351 (quoting Graver Tank, 339 U.S. at 608) (internal citation omitted); see Warner-Jenkinson, 520 U.S. at 39-40; Dawn Equip. Co. v. Kentucky Farms Inc., 140 F.3d 1009, 1016 (Fed. Cir. 1998); Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1258 (Fed. Cir. 1989). This standard has been referred to as the "function-way-result test." See Interactive Pictures Corp. v. Infinite Pictures, Inc., 274 F.3d 1371, 1376-77 (Fed. Cir. 2001).

The doctrine of equivalents may be limited by prosecution history estoppel. That is, claim amendments or arguments made during prosecution may give rise to a rebuttable presumption of a general disclaimer of the territory between the patentee's original claim and the amended or discussed claim. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S.

722, 740 (2002); Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 344 F.3d 1359, 1369 (Fed. Cir. 2003); Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1574 (Fed. Cir. 1997). Thus, if a narrowing claim amendment is related to patentability, prosecution history estoppel presumptively bars the assertion of the excluded range of equivalents for the amended claim element in subsequent litigation. Warner-Jenkins, 520 U.S. at 33. Further, embodiments of the claimed invention that are disclosed in the patent's specification but not claimed are dedicated to the public. See Johnson & Johnston Assocs. v. R.E. Serv. Co., 285 F.3d 1046, 1054-55 (Fed. Cir. 2002). These principles limit the doctrine of equivalents because as between the patentee, who had the opportunity to obtain broader claims, and the public at large, it is the patentee who bears the cost of failing to seek protection for foreseeable embodiments of the claimed invention. See Sage Prods., Inc. v. Devon Indus., Inc., 126 F.3d 1420, 1425 (Fed. Cir. 1997).

Finally, even if an infringer obtains a patent covering the accused product, a finding of infringement under the doctrine of equivalents may still be warranted. See Fiskars, Inc. v. Hunt Mfg. Co., 221 F.3d 1318, 1324 (Fed. Cir. 2000); Bio-Technology Gen. Corp. v. Genentech, Inc., 80 F.3d 1553, 1559 (Fed. Cir. 1996).

2. Application

As discussed supra, this Court finds that calcium trisodium DTPA is equivalent to the edetate in the asserted claims. Further, the amount of calcium trisodium DTPA in the accused product is equivalent to the amount of edetate recited in Claims 16-19 and 21-32 of the asserted patents and Claim 39 in the '520 patent. Finally, the calcium trisodium DTPA in Mayne's formulation is equivalent to the disodium edetate in Claims 2 and 20, and the amount of disodium edetate specified in Claim 34.

Mayne argues that AstraZeneca may not assert any range of equivalents for the asserted claims, because during prosecution it narrowed the claim term "edetate" to overcome the Patent Examiner's rejection in light of the Patel reference. Although prosecution history estoppel may limit the doctrine of equivalents, it does not limit the scope of the term edetate in this case. As this Court noted in its Markman ruling, AstraZeneca did not limit the meaning of edetate by argument or amendment. AstraZeneca, 352 F. Supp. 2d at 414. The amendments based on which Mayne argues for a narrow definition of "edetate" addressed the amount of edetate necessary and more precisely defined the microbiological test, but left the definition of edetate intact. AstraZeneca, 352 F. Supp. 2d at 414; see Interactive Pictures, 274 F.3d at 1376-77.

Mayne also contends that AstraZeneca's amendment narrowed the definition of edetate because it "excluded from its scope sodium calcium edetate, a salt of EDTA touted in the patents' specification as having 'some advantages over other additives.'" (Mayne Mem. at 49.) However, the test results in the specification on which Mayne relies are different from the claimed test conditions. (See Tr. at 794-96; 869-72; see PX 1, Col. 9, lines 41-50.) There is no evidence that sodium calcium edetate would fail the claimed test. Indeed, the fact that calcium trisodium DTPA passed the claimed test (JPTO ¶¶ VI.B.21-23) would suggest otherwise. Thus, there is no basis to conclude that, after the amendment, "edetate . . . encompasses a different, smaller group of compounds." (See Mayne Mem. at 13.)

Further, this Court concludes that the antimicrobial activity of calcium trisodium DTPA was unforeseeable during prosecution and, therefore, the patentees' failure to expressly claim it was not fatal. See Festo, 344 F.3d at 1365 n.2 ("[W]hen the narrowing amendment was made . . . is the relevant time for evaluating unforeseeability, for that is when the patentee presumptively surrendered the subject matter in question and it is at that time that foreseeability

is relevant."). Moreover, as Mayne itself argued to the USPTO during prosecution of its '108 patent, the antimicrobial activity of DTPA was unforeseeable despite the '520 patent's disclosure of the properties of edetate. (Tr. at 953-54; DX 152, Col. 1, lines 9-43, 53-57; DX 153 at FPC207734, FPC207742-43, FPC207746.) Additionally, reliance on the '701 patent (issued to Furia) is improper in this context, because it relates to a different field from the asserted patents. See Festo, 344 F.3d at 1369.

This Court also concludes that claims to calcium trisodium DTPA were not dedicated to the public. (See Mayne Mem. at 50.) Under Federal Circuit law, disclosed but unclaimed embodiments of the claimed invention are dedicated to the public. See Johnson & Johnston, 285 F.3d at 1054-55. In Johnson & Johnston, the patentees had disclosed various alternative materials for the substrate recited in the claim. 285 F.3d at 1050. However, the claim only recited the alternative embodiment of aluminum. Id. at 1055. Here, the argument that the inventors should have claimed "the broad class of metal ion sequestering agents" (Mayne Mem. at 14-15) is misplaced, because the claims require edetate. Had the claims recited EDTA – instead of edetate – Mayne's argument might be more persuasive. Further, the passage in the asserted patents to which Mayne cites for its argument that calcium trisodium DTPA cannot be the edetate in the claims is a discussion of the Glen UK patent (PX 1, Col. 3, lines 33-41), not the claimed invention. Thus, this passage did not result in a disclaimer of calcium trisodium DTPA or any other equivalent of edetate.

Additionally, this Court concludes that even though calcium trisodium DTPA can work at a lower concentration than EDTA, it still is an equivalent. (See Mayne Mem. at 16-17.) The asserted claims place an upper limit on the amount of edetate necessary; there is no lower limit except that there be some amount sufficient to pass the microbiological test. AstraZeneca,

352 F. Supp. 2d at 414. Indeed, as AstraZeneca asserts, a "formulation that works with a lower concentration than the edetate of the illustrative embodiment is literally within the claimed amount. Improved infringement is still infringement." (AstraZeneca's Response to Mayne's Proposed Findings of Fact and Conclusions of Law, dated Apr. 18, 2005 ("AstraZeneca Opp.") at 7-8.)

Further, despite Mayne's patent covering its accused formulation, a finding of infringement under the doctrine of equivalents is not precluded. Fiskars, 221 F.3d at 1324; Bio-Technology, 80 F.3d at 1559. Although the existence of a patent covering Mayne's formulation may be one factor to consider in the equivalence analysis, see Fiskars, 221 F.3d at 1324; Hoechst Celanese Corp. v. BP Chem. Ltd., 78 F.3d 1575, 1582 (Fed. Cir. 1996), it does not outweigh the substantial evidence of equivalence between Mayne's calcium trisodium DTPA and the claimed edetate.

This Court concludes that the differences between calcium trisodium DTPA and the claimed edetate are insubstantial to one of ordinary skill in the art because calcium trisodium DTPA satisfies the "function-way-result" test. See Lighting World, Inc. v. Birchwood Lighting, Inc., 382 F.3d 1354, 1357 (Fed. Cir. 2004); Boehringer Ingelheim, 320 F.3d at 1351 ("Under the doctrine of equivalents, a claim limitation not literally met may be satisfied by an element of the accused product if the differences between the two are 'insubstantial' to one of ordinary skill in the art."). Thus, the calcium trisodium DTPA in Mayne's generic propofol emulsion is equivalent to edetate in the asserted claims.

Accordingly, this Court concludes that Mayne's generic propofol formulation infringes Claims 1-14, 16-32 and 34 of the asserted patents as well as Claims 38 and 39 of the '520 patent under the doctrine of equivalents.

IV. Validity of the Asserted Patents

An issued patent is presumed valid.[17] 35 U.S.C. § 282. Thus, the accused infringer bears the burden of proving invalidity by clear and convincing evidence. 35 U.S.C. § 282; Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1348 (Fed. Cir. 2004); Oakley, Inc. v. Sunglass Hut Int'l, 316 F.3d 1331, 1339 (Fed. Cir. 2003). The burden of proving invalidity "is 'especially difficult' when, as is the present case, the infringer attempts to rely on prior art that was before the patent examiner during prosecution." Glaxo, 376 F.3d at 1348 (quoting Al-Site Corp. v. VSI Int'l Inc., 174 F.3d 1308, 1323 (Fed. Cir. 1999)); Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1467 (Fed. Cir. 1990); see Am. Hoist & Derrick Co. v. Sowa & Sons, Inc., 725 F.2d 1350, 1359 (Fed. Cir. 1984).

A. Anticipation

1. General Principles

A patent claim is invalid if the invention is anticipated by a public use or prior art reference – that is, if each limitation of that claim is found, either expressly or inherently, in a single public use or prior art reference. 35 U.S.C. § 102(a); Akamai Techs., Inc. v. Cable & Wireless Internet Servs., Inc., 344 F.3d 1186, 1192-93 (Fed. Cir. 2003); Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1576-77 (Fed. Cir. 1991). "[T]he dispositive question regarding anticipation is whether one skilled in the art would reasonably understand or infer from the prior art reference's teaching that every claim [limitation] was

[17] This Court concludes that the asserted patents comply with 35 U.S.C. § 112. See also AstraZeneca, 352 F. Supp. 2d at 414.

disclosed in that single reference." Dayco Prods., Inc. v. Total Containment, Inc., 329 F.3d 1358, 1368 (Fed. Cir. 2003) (internal quotation marks and alterations omitted).

"[A] prior art reference may anticipate when the claim limitation or limitations not expressly found in the reference are nonetheless inherent in it." MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365 (Fed. Cir. 1999). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1347 (Fed. Cir. 1999). It is irrelevant that those of ordinary skill in the art failed to recognize the inherent characteristics. In re Cruciferous Sprouts Litig., 301 F.3d 1343, 1350 (Fed. Cir. 2002); Atlas Powder, 190 F.3d at 1347. Rather, "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder, 190 F.3d at 1347 (citations omitted). Further, a claim element reciting a numerical range is anticipated by a reference that discloses any portion of that range. Scaltech, Inc. v. Retec/Tetra, LLC, 269 F.3d 1321, 1330 (Fed. Cir. 2001); Titanium Metals Corp. of Am. v. Banner, 778 F.2d 775, 782 (Fed. Cir. 1985) ("It is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if one of them is in the prior art.").

Anticipation is a question of fact, Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research, 346 F.3d 1051, 1054 (Fed. Cir. 2003), as is the question of whether a prior art reference inherently discloses a patent claim limitation, Atlas Powder, 190 F.3d at 1346.

2. Application

The USPTO considered the Glen UK patent on which Mayne relies for its anticipation argument, and concluded that it did not teach the claimed invention. As already noted, the Glen UK patent does not address the problem of microbial contamination or suggest adding a small amount of edetate to an oil-in-water emulsion to retard microbial growth. There is no mention in the Glen UK patent of the claimed test to determine whether growth had been sufficiently retarded or of the methods claimed in the '355 and '356 patents. Thus, because there is no evidence that the Glen UK patent's compositions control microbial growth, they do not practice the methods claimed in the '355 and '356 patents. See Merck & Co. v. Teva Pharmaceuticals USA, Inc., 347 F.3d 1367, 1372 (Fed. Cir. 2003).

Moreover, Examples 2 and 3 in the Glen UK patent do not disclose propofol dissolved in a water-immiscible solvent, a requirement of each of the asserted claims. Further, those exemplary formulations in the Glen UK patent do not involve an oil-in-water emulsion, but instead a micro-emulsion. In view of the substantial differences between the disclosure in the Glen UK patent and the claimed propofol formulation, this Court concludes that the principle of inherency is inapplicable. See Trintec Indus., Inc. v. Top-U.S.A. Corp., 295 F.3d 1292, 1295 (Fed. Cir. 2002) (noting that inherency applies when the missing element is "necessarily present" in the prior art). Because the Glen UK patent, at best, provides "a place to start for formulators" (Tr. at 694-95, 830-32), it does not anticipate. Dewey & Almy Chem. Co. v. Mimex Co., 124 F.2d 986, 989 (2d Cir. 1942) (L. Hand, J.) ("If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, it does not inform the art without more how to practice the new invention . . . and it is not an

anticipation."); Akzo N.V. v. United States, Int'l Trade Comm'n, 808 F.2d 1471, 1479 (Fed. Cir. 1986); see In re Arkley, 455 F.2d 586, 587-88 (C.C.P.A. 1972).

Accordingly, this Court concludes that the Glen UK patent does not anticipate the claimed invention.

B. Obviousness

1. General Principles

A patent claim is invalid if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); Merck v. Teva, 395 F.3d 1364, 1372-78 (Fed. Cir. 2005); Ryko Mfg. Co. v. Nu-Star, Inc., 950 F.2d 714, 716 (Fed. Cir. 1991). Unlike anticipation, an obviousness inquiry involves examining the combination of elements in multiple prior art references. The ultimate determination of obviousness is a question of law that turns on the underlying facts. Sandt Tech. Ltd. v. Resco Metal & Plastics Corp., 264 F.3d 1344, 1354 (Fed. Cir. 2001). The fact finder must consider "1) the scope and content of the prior art; 2) the differences between the prior art devices and the claimed invention; 3) the level of ordinary skill in the art; and 4) objective considerations, such as commercial success, long felt need, failure of others, and copying." Sandt, 264 F.3d at 1354 (citing Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966)); Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1343 (Fed. Cir. 2000); Ecolochem, Inc. v. S. Cal. Edison Co., 227 F.3d 1361, 1371 (Fed. Cir. 2000).

For a patent to be invalid for obviousness based "on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references."

In re Rouffet, 149 F.3d 1350, 1355 (Fed. Cir. 1998) (citing In re Geiger, 815 F.2d 686, 688 (Fed. Cir. 1987)); ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577 (Fed. Cir. 1984). Such motivation must be established by clear and convincing evidence. In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999); In re Rouffet, 149 F.3d at 1357-58. The suggestion to combine references may flow from the problem itself, see Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573 (Fed. Cir. 1996), or from "teachings of the prior art, and the knowledge of persons of ordinary skill in the art." In re Rouffet, 149 F.3d at 1357. Thus, "[w]hen determining the patentability of a claimed invention which combines two known elements, 'the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination.'" In re Beattie, 974 F.2d 1309, 1311-12 (Fed. Cir. 1992) (quoting Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1462 (Fed. Cir. 1984)).

35 U.S.C. § 102, as limited by 35 U.S.C. § 103(c), defines prior art for purposes of an obviousness analysis. Only "analogous art" may be considered. See Wang Labs., Inc. v. Toshiba Corp., 993 F.2d 858, 864 (Fed. Cir. 1993); In re Clay, 966 F.2d 656, 658-59 (Fed. Cir. 1992). To constitute analogous art, a prior art reference must (1) be "from the same field of endeavor [as the invention], regardless of the problem addressed," and (2) if the reference is not from the same field, it must be "reasonably pertinent to the particular problem with which the inventor is involved."[18] In re Clay, 966 F.2d at 658-59. A reference is reasonably pertinent if it "'logically would have commended itself to an inventor's attention in considering his problem.'" Wang, 993 F.2d at 864 (quoting In re Clay, 966 F.2d at 659).

[18] Thus, the '701 patent and its file history, which is not analogous art, need not be considered.

The claimed invention as a whole must be compared to the prior art as a whole, Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1383 (Fed. Cir. 1986); Hodosh v. Block Drug Co., 786 F.2d 1136, 1143 n.5 (Fed. Cir. 1986), and courts must avoid aggregating pieces of prior art through hindsight which would not have been combined absent the inventors' insight. See Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH, 139 F.3d 877, 880 (Fed. Cir. 1998); W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1552-53 (Fed. Cir. 1983) ("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher."). As a further check against hindsight analysis, the Court must consider "secondary considerations" of nonobviousness. Ruiz v. A.B. Chance Co., 234 F.3d 654, 662-63, 667 (Fed. Cir. 2000). These considerations include evidence of commercial success, long-felt but unsolved need for the invention, unexpected results and copying by the infringer. Dann v. Johnston, 425 U.S. 219, 230 n.4 (1976); Graham, 383 U.S. at 17; Syntex (U.S.A.) LLC v. Apotex, Inc., 407 F.3d 1371, 1378 (Fed. Cir. 2005); Ruiz, 234 F.3d at 667.

2. Application

Based on the evidence, this Court concludes that Mayne has not established by clear and convincing evidence that there is a suggestion in the art to combine any prior art reference with the Glen UK patent, or that one of ordinary skill in the art would be motivated to make such a combination. While Mayne proffered evidence to show that the individual elements of the claimed invention were known in the art, the prior art does not suggest the addition of edetate to an oil-in-water emulsion for injection in human patients. It is irrelevant that the

individual elements of a claim are known, unless there is a suggestion to combine them. Life Techs., Inc. v. Clontech Labs., Inc., 224 F.3d 1320, 1326 (Fed. Cir. 2000) ("It is axiomatic that a claimed invention is not obvious solely because it is composed of elements that are all individually found in the prior art. . . . For the Johnson article to render the claimed invention obvious, there must have been, at the time the invention was made, a reasonable expectation of success in applying Johnson's teachings."); Jones v. Hardy, 727 F.2d 1524, 1529-30 (Fed. Cir. 1984).

The pertinent prior art on which Mayne relies was before the Patent Examiner. As Goldberg opined prior to this litigation, the patentees "legitimate[ly]" distinguished [the prior art] from the claimed inventions," and, as a result, "a properly informed Court would find this cited art insufficient to invalidate the claims." (Tr. at 537-39; JX 25 at FPC251527-29; JX 26 at FPC252294.) Finally, evidence of Modified Diprivan's commercial success and ESI's configuring its formulation by using the claimed invention as a blueprint further establish nonobviousness. Dann, 425 U.S. at 230 n.4; Graham, 383 U.S. at 17; Syntex (U.S.A.), 407 F.3d at 1378; Ruiz, 234 F.3d at 667.

Accordingly, this Court concludes that the asserted claims would not have been obvious at the time those inventions were made.

V. Enforceability of the Asserted Patents

A. General Principles

A patent may be unenforceable if it is the product of inequitable conduct. "Inequitable conduct occurs when a patent applicant breaches his or her 'duty of candor and good faith' to the PTO." Novo Nordisk Pharms., Inc. v. Bio-Technology Gen. Corp., --- F.3d ---, 2005

WL 2443857, at *10 (Fed. Cir. Oct. 05, 2005) (quoting 37 C.F.R. § 1.56(a)); see Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs., Ltd., 394 F.3d 1348, 1351 (Fed. Cir. 2005). "Inequitable conduct requires proof that a patent applicant did not disclose material information to the PTO with intent to deceive." CFMT, Inc. v. YieldUp Int'l Corp., 349 F.3d 1333, 1340 (Fed. Cir. 2003) (citing Kingsdown Med. Consultants, Ltd. v. Hollister Inc., 863 F.2d 867, 872 (Fed. Cir. 1988)). Inequitable conduct may include an "affirmative misrepresentation of a material fact, failure to disclose material information, or submission of false material information, coupled with an intent to deceive." Molins PLC v. Textron, Inc., 48 F.3d 1172, 1178 (Fed. Cir. 1995); see also CFMT, 349 F.3d at 1340. "Both intent and materiality are questions of fact that must be proven by clear and convincing evidence." Dayco Prods., 329 F.3d at 1362; see CFMT, 349 F.3d at 1340.

The inequitable conduct analysis is performed in two steps: "first, a determination of whether the [conduct] meets a threshold level of materiality and intent to mislead, and second, a weighing of the materiality and intent in light of all the circumstances to determine whether the applicant's conduct is so culpable that the patent should be held unenforceable." Purdue Pharma L.P. v. Boehringer Ingelheim GMBH, 237 F.3d 1359, 1366 (Fed. Cir. 2001) (internal quotations and alterations omitted); Dayco Prods., 329 F.3d at 1363. If one claim of a patent is found unenforceable on grounds of inequitable conduct, the entire patent is unenforceable. J.P. Stevens & Co. v. Lex Tex Ltd., 747 F.2d 1553, 1561 (Fed. Cir. 1984).

Under 37 C.F.R. § 1.56(b), information is material if it is "not cumulative to information already of record" and (1) establishes a prima facie case of unpatentability of a claim or (2) refutes or is inconsistent with a position taken by the applicant (i) in response to an

argument of unpatentability by the PTO or (ii) in asserting patentability.[19] See Purdue Pharma L.P. v. Endo Pharms. Inc., 410 F.3d 690, 696 (Fed. Cir. 2005); Bruno Indep., 394 F.3d at 1352-53; Dayco Prods., 329 F.3d at 1363-64. A withheld prior art reference may be highly material when it discloses a more complete combination of relevant features, even if those features are before the patent examiner in other references. Molins, 48 F.3d at 1180. However, information that does not affect patentability is not material. See Frazier v. Roessel Cine Photo Tech, Inc., 417 F.3d 1230, 1237-39 (Fed. Cir. 2005) (holding that because an advertisement did not affect patentability, the patentees' failure to disclose it was not material); Northern Telecom, Inc. v. Datapoint Corp., 908 F.2d 931, 940 (Fed. Cir. 1990) ("Since the Viatron 21 device was not prior art, it was not material to patentability."); Envtl. Designs, Ltd. v. Union Oil Co. of Cal., 713 F.2d 693, 698 (Fed. Cir. 1983) ("There was no duty . . . to bring to the attention of the [USPTO] the Riesenfeld disclosure because it was a mere 'conception' and was admittedly not prior art."). "An applicant can not be guilty of inequitable conduct if the reference was cited to the examiner, whether or not it was a ground of rejection by the examiner." Fiskars, Inc. v. Hunt Mfg. Co., 221 F.3d 1318, 1327 (Fed. Cir. 2000); see 37 C.F.R. § 1.56(a). The Patent Examiner is presumed to have read and understood the art cited during the prosecution of a patent. Am. Hoist, 725 F.2d at 1359. Arguments by patentees advocating a particular interpretation of the prior art, "which the [Patent] Examiner [is] free to accept or reject," do not rise to the level of a material misrepresentation. See Life Techs., 224 F.3d at 1326.

"Intent need not, and rarely can, be proven by direct evidence." Merck & Co. v. Danbury Pharmacal, Inc., 873 F.2d 1418, 1422 (Fed. Cir. 1989). "Rather, in the absence of a

[19] "According to the [USPTO's] notice of final rulemaking, the rule change applied to all applications pending or filed after March 16, 1992." Bruno Indep., 394 F.3d at 1352 (citing Duty of Disclosure, 57 Fed. Reg. 2021 (Jan. 17, 1992)).

credible explanation, intent to deceive is generally inferred from the facts and circumstances surrounding a knowing failure to disclose material information." Bruno Indep., 394 F.3d at 1354 (citing Paragon Podiatry Lab., Inc. v. KLM Labs. Inc., 984 F.2d 1182, 1193 (Fed. Cir. 1993)). An inference of intent to deceive is based on the totality of the circumstances, including the nature of the conduct and evidence of the presence or absence of good faith. Li Second Family L.P. v. Toshiba Corp., 231 F.3d 1373, 1379-80 (Fed. Cir. 2000); Perseptive Biosys., Inc. v. Pharmacia Biotech., Inc., 225 F.3d 1315, 1321-22 (Fed. Cir. 2000). Gross negligence alone is insufficient to establish intent. Kingsdown, 863 F.2d at 876; see Baxter Int'l, Inc. v. McGaw, Inc., 149 F.3d 1321, 1329 (Fed. Cir. 1998).

"As a general principle, materiality and intent are balanced–a lesser quantum of evidence of intent is necessary when the omission or misrepresentation is highly material, and vice versa." Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1358 (Fed. Cir. 2003); see Li Second Family, 231 F.3d at 1378 ("The more material the information misrepresented or withheld by the applicant, the less evidence of intent will be required in order to find that inequitable conduct has occurred."). "At the same time, however, there must be some threshold showing of intent to be balanced; [courts] will not find inequitable conduct on an evidentiary record that is completely devoid of evidence of the patentee's intent to deceive the [USPTO]." Amgen, 314 F.3d at 1358.

Finally, "[w]hen both materiality and deceptive intent have been established by clear and convincing evidence, decision of the ultimate issue of inequitable conduct is within the discretion of the district court." Norian Corp. v. Stryker Corp., 363 F.3d 1321, 1331 (Fed. Cir. 2004); Monsanto Co. v. Bayer Bioscience N.V., 363 F.3d 1235, 1239 (Fed. Cir. 2004) ("Once the challenger has shown the requisite levels of materiality and intent, the district court must

balance the equities to determine whether the patentee has committed inequitable conduct that warrants holding the patent unenforceable.").

B. Application

This Court concludes that information relating to AstraZeneca's internal unpublished work on formulations that retarded microbial growth without the use of edetate was not material to the prosecution of the asserted patents. First, these works were not prior art under 35 U.S.C. § 102. Second, even if AstraZeneca's internal unpublished work was prior art, it would be irrelevant to the claims of the patents, since the claimed formulations require edetate. Mayne's suggestion that AstraZeneca should have informed the Patent Examiner of propofol's antimicrobial properties misses the mark because that information was part of the record before the USPTO. Moreover, even if the information was not before the USPTO, it is irrelevant to the claims which relate to the antimicrobial properties of edetate – not propofol.

With respect to Mayne's contention that AstraZeneca made improper arguments to the USPTO to distinguish the Glen UK patent and the Patel reference, Rule 56(a) states that the duty of disclosure "is deemed to be satisfied" if all material information is cited in an Information Disclosure Statement or Form 1449. Fiskars, 221 F.3d at 1327. There is no dispute that the Glen UK patent and the Patel reference were both disclosed to the USPTO. The patentees' interpretation regarding the prior art references do not constitute material misrepresentations because the Patent Examiner was free to accept or reject those arguments and draw his own conclusions from the prior art before him. See Life Techs., 224 F.3d at 1326.

In any event, there is no evidence of the patentees' intent to deceive the USPTO. Even if this Court were to conclude that AstraZeneca withheld material information, this Court

cannot infer a bad faith intent from such a failure to disclose without some additional evidence.[20] Amgen, 314 F.3d at 1358. Accordingly, because this Court concludes that the patentees are not guilty of inequitable conduct, the asserted patents are enforceable.

VI. Attorney Fees

A. General Principles

In exceptional cases, the Court may award reasonable attorney fees to the party prevailing in a patent infringement action. 35 U.S.C. § 285. The determination of whether a case is exceptional is a factual determination for which the patentee bears the burden of proof by clear and convincing evidence. Crystal Semiconductor Corp. v. TriTech Microelectronics Int'l, Inc., 246 F.3d 1336, 1351 (Fed. Cir. 2001); Yamanouchi Pharm., 231 F.3d at 1346-47. To determine whether a case is exceptional, a trial court must look at the totality of the circumstances. Yamanouchi, 231 F.3d at 1347.

As discussed above, 35 U.S.C. § 271(e)(2) creates an artificial act of infringement for purposes of establishing jurisdiction in the federal courts. Thus, the mere filing of "an ANDA application or certification cannot support a finding of willful infringement for purposes of awarding attorney's fees." Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1350-51 (Fed. Cir. 2004). Similarly, the making of Paragraph IV Certifications cannot support a finding of willful infringement. See Aventis Pharm. v. Cobalt Pharm., Inc., 355 F. Supp. 2d 586, 590-93

[20] This Court declines Mayne's invitation to infer intent to deceive from Mr. Platt's failure to testify at trial. Prior to the trial, this Court denied Mayne's motion to compel Mr. Platt's attendance because he lives in Great Britain – beyond the subpoena power of the Court, and because Mr. Platt is not a current AstraZeneca employee. See Fed. R. Civ. P. 45(c)(3); Price Waterhouse LLP v. First Am. Corp., 182 F.R.D. 56, 61 (S.D.N.Y. 1998); Zeeck v. Melina Taxi Co., 177 A.D.2d 692, 694, 576 N.Y.S.2d 878 (2d Dep't 1991). Because Mayne was allowed to use Mr. Platt's video deposition at trial, there was no prejudice to Mayne.

(D. Mass. 2005). However, the filing of an ANDA along with other misconduct may support a finding that a case is exceptional for purposes of 35 U.S.C. § 285. See Yamanouchi, 231 F.3d at 1346-47. Such misconduct may "include willful infringement, . . . offensive litigation tactics, vexatious or unjustified litigation, or frivolous filings." Yamanouchi, 231 F.3d at 1346-47; see also Phonometrics, Inc. v. Westin Hotel Co., 350 F.3d 1242, 1246-48 (Fed. Cir. 2003).

Even if a court finds a case "exceptional" under the statute, it must exercise discretion in determining whether an award of attorney fees is warranted. See Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1370 (Fed. Cir. 1999); see also Graco, Inc. v. Binks Mfg. Co., 60 F.3d 785, 794-95 (Fed. Cir. 1995) ("A finding by a court that a case is exceptional is a factual determination . . . whereas the decision to award fees is discretionary."). A number of factors determine whether attorney's fees are appropriate, including the "closeness of the case, tactics of counsel, the conduct of the parties and any other factors that may contribute to a fairer allocation of the burdens of litigation as between winner and loser." J.P. Stevens Co. v. Lex Tex Ltd., 822 F.2d 1047, 1051 (Fed. Cir. 1987). Thus, "[a]ttorney fees are not to be routinely assessed against a losing party in litigation in order to avoid penalizing a party 'for merely defending or prosecuting a lawsuit,' and are awarded to avoid a gross injustice." Revlon, Inc. v. Carson Prods. Co., 803 F.2d 676, 679 (Fed. Cir. 1986) (quoting Fleischmann Distilling Corp. v. Maier Brewing Co., 386 U.S. 714, 718 (1967)).

B. Application

As already noted, after learning of the '520 patent, ESI modified its generic propofol emulsion by adding calcium trisodium DTPA, in part, because it believed that such modification would not infringe AstraZeneca's patents. (Tr. at 944-47; JX 4.) Further, Mayne

obtained opinion letters from its counsel prior to the filing of its original ANDA, the supplemental ANDA and the Paragraph IV certifications. Each opinion letter concluded that Mayne's formulation would not infringe AstraZeneca's claimed formulation. While Goldberg raised doubts about the invalidity position intimated in Heller's July 2000 opinion letter, he too opined that the product of the ANDA did not infringe the asserted patents. (Tr. at 547-48; JX 25.)

Mayne's filing of the ANDA was not improper merely because two attorneys disagreed on one legal issue (i.e., validity of the asserted patents), especially when all involved attorneys uniformly concluded that the product of the ANDA would not infringe the asserted patents. See American Med. Sys., Inc. v. Med. Eng'g Corp., 6 F.3d 1523, 1530 (Fed. Cir. 1993) ("A finding of willfulness requires the fact-finder to find that clear and convincing evidence shows 'that the infringer acted in disregard of the patent . . . [and] had no reasonable basis for believing it had a right to do the acts.'" (quoting Stickle v. Heublein, Inc., 716 F.2d 1550, 1565 (Fed. Cir. 1983))); Hall v. Aqua Queen Mfg., Inc., 93 F.3d 1548, 1555 (Fed. Cir. 1996) ("The test of willful infringement is 'whether, under all the circumstances, a reasonable person would prudently conduct himself with any confidence that a court might hold the patent invalid or not infringed.'" (quoting State Indus., Inc. v. Mor-Flo Indus., Inc., 883 F.2d 1573, 1581 (Fed. Cir. 1989) (emphasis added)).

In light of Mayne's reliance on its counsels' opinion letters, AstraZeneca has not provided clear and convincing evidence that Mayne's ANDA was improper. See Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1191 (Fed. Cir. 1998) ("It is well settled that an important factor in determining whether willful infringement has been shown is whether or not the infringer obtained the opinion of counsel."); In re Mahurkar Patent Litig., 831 F. Supp. 1354,

1395 (N.D. Ill. 1993), aff'd, 71 F.3d 1573 (Fed. Cir. 1995) ("[I]t [is] particularly difficult to infer willfulness when a layman receives and acts on legal advice."). Indeed, "cases where willful infringement is found despite the presence of an opinion of counsel generally involve situations where the opinion of counsel was either ignored or found to be incompetent." Read Corp. v. Portec, Inc., 970 F.2d 816, 829 (Fed. Cir. 1992). Here, Mayne did not ignore its counsels' opinions and AstraZeneca has not provided clear and convincing evidence that the Heller, Meloro and Goldberg opinion letters were incompetent.

Finally, Mayne's litigation conduct has not been baseless. While Mayne defended itself vigorously against charges of infringement and challenged the validity of the asserted patents, it did so with a good faith basis for each legal position advanced. See, e.g., Knorr-Bremse Systeme Fuer Nutzfahrzeuge GmbH v. Dana Corp., 372 F. Supp. 2d 833, 851-52 (E.D. Va. 2005); Mosinee Paper Corp. v. James River Corp. of Virginia, 22 U.S.P.Q.2d 1657, 1664 (E.D. Wis. 1992) (noting that the case was "not tried according to the usual patent case Marquis of Queensberry rules"); Morgan Adhesives Co. v. Chemtrol Adhesives, Inc., 574 F. Supp. 832, 836 (N.D. Ohio 1983), aff'd, 765 F.2d 158 (Fed. Cir. 1985); Leinoff v. Louis Milona & Sons, Inc., 556 F. Supp. 280, 284 (S.D.N.Y. 1983), rev'd on other grounds, 726 F.2d 734 (Fed. Cir. 1984) ("There may well be some merit to plaintiff's assertion that defendant was not justified in challenging this court's prior finding of the validity of plaintiff's patent. However, there is no evidence of bad faith, and this court is not willing to discourage attorneys from that vigorous representation of clients which their Code of Professional Responsibility demands of them.").

Therefore, this case is not exceptional under 35 U.S.C. § 285 and an award of attorney fees is not warranted.

CONCLUSION

Accordingly, this Court concludes that (1) Mayne's generic propofol formulation literally infringes Claims 1 and 3-14 of the asserted patents as well as Claim 38 of the '520 patent; (2) Mayne's generic propofol formulation infringes Claims 1-14, 16-32 and 34 of the asserted patents as well as Claims 38 and 39 of the '520 patent under the doctrine of equivalents; (3) the asserted claims are valid; (4) the asserted patents are enforceable; and (5) this case is not exceptional under 35 U.S.C. § 285.

The foregoing constitutes this Court's findings of fact and conclusions of law as required by Rule 52 of the Federal Rules of Civil Procedure.

The parties are directed to submit a final judgment consistent with this Opinion and Order within seven (7) business days.

Dated: November 2, 2005
New York, New York

SO ORDERED:

WILLIAM H. PAULEY III
U.S.D.J.

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